A1 cont.

June 11, 1999.

IN THE CLAIMS:

Please cancel Claims 6, 12 and 16 without prejudice.

Please amend Claims 1-5, 7-11, 13-15, and 17-18 as follows:

1. (Amended) A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising at least one DNA sequence encoding the specific iodine transporter (Na^+/I^- Symporter) NIS or a derivative thereof, wherein said DNA sequence is placed under the control of a transcriptional promoter allowing its expression in tumor cells.

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2. (Amended) The defective recombinant adenovirus of Claim 1, wherein the DNA sequence is a cDNA sequence.

3. (Amended) The defective recombinant adenovirus of Claim 1, wherein the DNA sequence is a gDNA sequence.

4. (Amended) The defective recombinant adenovirus of Claim 1, wherein the DNA sequence encodes the specific murine iodine transporter (Na^+/I^- Symporter) NIS.

5. (Amended) The defective recombinant adenovirus of Claim 1, wherein the DNA sequence encodes the specific human iodine transporter (Na^+/I^- Symporter) NIS.

7. (Amended) The defective recombinant adenovirus of Claim 1, wherein the transcriptional promoter is a viral promoter.

8. (Amended) A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising a cDNA sequence encoding the human iodine transporter NIS under the control of the CMV promoter.

9. (Amended) A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising a DNA sequence encoding the iodine transporter NIS or a derivative thereof under the control of a promoter allowing predominant expression in tumor cells.

10. (Amended) The defective recombinant adenovirus of Claim 9, wherein the promoter is selected from the group consisting of the regulatory sequence of the elastase I gene, the regulatory sequence of the insulin gene, the regulatory sequence of the gene for immunoglobulins, the regulatory gene of the mouse mammary tumor virus, the regulatory sequence of the PSA gene, the regulatory sequence of the alpha-fetoprotein gene, the regulatory sequence of the alpha 1-antitrypsin gene, the regulatory sequence of the β-globin gene, the regulatory sequence of the gene for basic myelin, the regulatory sequence of the gene for the myosin light chain 2, and the regulatory sequence of the gene for the gonadotrophin-releasing hormone.

11. (Amended) The defective recombinant adenovirus of Claim 1, further comprising a deletion of all or part of an E1 region, a deletion of all or part of an E4 region, or a deletion of all or part of the E1 region and a deletion of all or part of the E4 region.

13. (Amended) The defective recombinant adenovirus of Claim 1, wherein said adenovirus is a human adenovirus type Ad 2 or Ad 5 or a canine adenovirus type CAV-2.

14. (Amended) The defective recombinant adenovirus of Claim 1, further comprising at least one gene encoding a polypeptide involved in a peroxidase system.

15. (Amended) A pharmaceutical composition comprising said defective recombinant adenovirus of Claim 1 and a physiologically acceptable vehicle.

17. (Amended) The pharmaceutical composition of Claim 15, in injectable form.

18. (Amended) The pharmaceutical composition of Claim 15, comprising between 10^4 and 10^{14} pfu/ml defective recombinant adenoviruses, inclusive.

Please add the following New Claims:

--19. The defective recombinant adenovirus of Claim 7, wherein the viral promoter is selected from the group consisting of E1A, MLP, CMV, RSV-LTR, MT-1, and SV40.

20. The defective recombinant adenovirus of Claim 14, wherein said gene encoding a polypeptide involved in a peroxidase system comprises the gene for glucose oxidase or the gene for thyroperoxidase.

21. The pharmaceutical composition of Claim 18, comprising between 10^6 to 10^{11} pfu/ml defective recombinant adenoviruses, inclusive.

22. The defective recombinant promoter of Claim 4, further comprising a deletion of all or part of an E1 region, a deletion of all or part of an E4 region, or a deletion of all or part of the E1 region and a deletion of all or part of the E4 region.

23. The defective recombinant promoter of Claim 4, further comprising a gene encoding a polypeptide involved in the peroxidase system.

24. The defective recombinant promoter of Claim 5, further comprising a deletion of all or part of an E1 region, a deletion of all or part of an E4 region, or a deletion of all or part of the E1 region and a deletion of all or part of the E4 region.

25. The defective recombinant virus of Claim 5, further comprising further comprising a gene encoding a polypeptide involved in the peroxidase system.

26. The defective recombinant adenovirus of Claim 8, further comprising a deletion

of all or part of an E1 region, a deletion of all or part of an E4 region, or a deletion of all or part of the E1 region and a deletion of all or part of the E4 region.

27. The defective recombinant adenovirus of Claim 8, further comprising at least one gene encoding a polypeptide involved in a peroxidase system.

28. The defective recombinant adenovirus of Claim 9, further comprising a deletion of all or part of an E1 region, a deletion of all or part of an E4 region, or a deletion of all or part of the E1 region and a deletion of all or part of the E4 region.

29. The defective recombinant adenovirus of Claim 9, further comprising at least one gene encoding a polypeptide involved in a peroxidase system.

30. A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising a DNA sequence that encodes a specific murine iodine transporter (Na^+/I^- Symporter) NIS or a specific human iodine murine iodine transporter (Na^+/I^- Symporter) NIS, wherein said DNA sequence is placed under the control of a transcription promoter allowing its expression in tumor cells.

31. The defective recombinant adenovirus of Claim 30, wherein said defective recombinant adenovirus comprises a deletion of all or a part of an E1 region, a deletion of all or part of an E4 region, or a deletion of all or part of the E1 region and a deletion of all or part of the

E4 region.

32. The defective recombinant adenovirus of Claim 31, wherein said defective recombinant adenovirus comprises a gene that encodes a polypeptide involved in the peroxidase system.

33. A method for treating cancer in a subject comprising the steps of:

(a) administering to the subject the recombinant defective adenovirus of Claim 1; and

(b) administering to the subject a radioactive isotope of iodine

34. The method of Claim 33, further comprising the step of administering an anti-cancer agent to the subject.

35. The method of Claim 34, wherein the anti-cancer agent comprises a taxoid, a derivative of platinum, cis-platin, etoposide, etoposide phosphate, bleomycin, mitomycin C, CCNU, doxorubicin, daunorubicin, idarubicin, or ifosfamide.

36. A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising:

(a) a DNA sequence that:

(i) encodes for a specific murine iodine transporter (Na^+/I^- Symporter) NIS that is under the control of a transcriptional promoter that allows

expression of said DNA sequence in tumor cells; or

(ii) encodes for a specific human iodine transporter (Na^+/I^- Symporter) NIS that is under the control of a transcriptional promoter that allows expression of said DNA sequence in tumor cells;

(b) a deletion of all or part of an E1 region, a deletion of all or part of an E2 region, or a deletion of all or part of the E1 region and a deletion of all or part of the E2 region; and

(c) a gene encoding a polypeptide involved in a peroxidase system.

37. A method for treating cancer in a subject comprising administering to the subject the defective recombinant adenovirus of Claim 36, and a radioactive isotope of iodine.

38. The method of Claim 37, further comprising administering an anti-cancer agent to the subject.--

REMARKS

Claims 1-18 are presently pending in this case. In this preliminary amendment, Applicants have canceled Claims 6, 12 and 16, without prejudice, have amended Claims 1-5, 7-11, 13-15, and 17-18, and have added new Claims 19-38. Applicants have also amended the instant Specification to include a Priority Claim. Support for amended Claims 1-5, 7-11, 13-15, and 17-18, as well as new Claims 19-38, can be found generally throughout the instant Specification, particularly at pages 27-28 and Claims 1-18 as filed. Consequently, the instant Amendment introduces no new matter into the instant Application. Attached hereto is a marked-